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08/509,359

APPLICATION NO.	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/509,359	07/31/95	ST. GEORGE-HYSLOP	P CAN-004

HM21/0608

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EXAMINER	
DUFFY, P	
ART UNIT	**PAPER NUMBER**
1645	24

DATE MAILED: 06/08/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 2-23-98

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 24, 71, 73-79 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 24, 71, 74, 77-79 is/are rejected.

☒ Claim(s) 73, 75, 76 is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Notice to Comply.

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

Response to Amendment

1. The Group and/or Art Unit of U.S. Patent application S.N. 08/509,359 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Technology Center 1600, Group 1640, Art Unit 1645.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

3. The amendment filed 2-23-98 has been entered into the record with the exception of the numerous changes requested to the specification, see paragraph 4 below. Claims 71 and 73-79 are pending and under examination.

New Objections Based on Amendment

4. A substitute specification including claims is required pursuant to 37 CFR 1.125(a) because the number of amendments to the specification will present difficulty in arranging the papers for printing an accurate representation of the specification.

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

Objections and /or Rejections Maintained

5. The objection to the disclosure as containing sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2) is maintained for the reason(s) set forth on the attached Notice To Comply With The Sequence Rules or CRF Diskette Problem Report. Appropriate correction is required.

6. The rejection of claims 24, 71, 74 and 77-79 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for E5-1 proteins having the sequence of SEQ ID NO:138 (wild type protein) and SEQ ID NO:138 wherein the Asn at amino acid position 141 has been replaced by Ile and/or wherein the Met at amino acid position 239 has been replaced by Val (naturally occurring mutants), does not reasonably provide enablement for other mammalian and human E5-1 proteins, mutations, and splice variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims is **maintained for reasons made of record** for claims 24-25, 71-72 and 74-76 in Paper No.20, mailed 8-21-97.

Applicants' arguments have been carefully considered but are not persuasive for the reasons set forth below. Applicants' assert that the specification teaches the normal and mutant mammalian E5-1 proteins of the present invention. This is not persuasive because the specification sets forth a single mammalian species, the wild type human sequence represented by SEQ ID NO:138 and specific mutations thereof. The specification provides no written description of any other mammalian E5-1 wild type protein, no written description of any mutant of any other mammalian protein. The disclosure of a single species does not support a genus

claim. Applicants allege that the specification teaches that disease mechanisms insights and therapies analogous to those described in relation to the ARMP gene. This is not persuasive because the ARMP gene and protein are independent from the E5-1 gene and protein, the proteins are encoded by different genes on different chromosomes. Moreover, Alzheimer's is a uniquely human disease and therefore disease treatments of mammals other than humans offers no insight to this uniquely human disease. Applicants indicate that the case law citations cited by the examiner are not on point since they are drawn to DNA sequences and not to proteins. This is not persuasive because the underling issue is whether the written description of a single species supports the broad class of "mammalian", in an unpredictable art, absent undue experimentation. The specification fails to identify common identifying characteristics for a substantial portion of the genus, such that one skilled in the art could reasonably predict the general structure of the species within the claimed genus. Applicants' allege that they teach how to identify other proteins (i.e. make) without undue experimentation and cite page 34 lines 3-23. This is not persuasive because applicant's have failed to teach how to make and use other proteins within the broad class of mammalian E5-1 proteins because I) the specification fails to teach that species homologues are indeed present for this specific protein, ii) the specification fails to teach conserved regions of the E5-1 protein which could be used to generate antibodies or develop cloning strategies for the mammalian E5-1 equivalents instantly claimed and iii) since, Alzheimer's is a uniquely human disease, it is not therefore readily apparent that E5-1 species homologues would be present in other mammalian species. Thus, the disclosure of a single species does not enable making the genus. As to page 34 lines 3-23, this passage is not persuasive because applicants specification demonstrates that the human ARMP protein and human E5-1 protein are not encoded by the same gene. Thus, consensus sequences and

methodology disclosed at page 34, would not predictably and reproducibly apply to the E5-1 genus. Applicants have not demonstrated that equivalent protein E5-1 homologs are present in other mammalian species, present no cloning or protein consensus sequences for the genus which could predictably and reproducibly identify or species homologues, absent undue experimentation. The specification fails to provide consensus sequences or other guidance so as to guide one skilled in the art to purify other E5-1 species protein homologs. Thus, clearly applicants did not disclose a genus of E5-1 mammalian polypeptides, nor is the specification enabling for making the scope of variants and mutants claimed. Moreover, the specification fails to teach how to use the other mammalian E5-1 proteins, mutants and splice variants. No specific disease has been associated with the E5-1 protein other than Alzheimer's disease. No specific function of the E5-1 protein is set forth in the specification. Thus, even if the skilled artisan could make the E5-1 protein from other mammals, how would these proteins then be used ? As previously set forth ".. it may be inferred from the specification that antibodies to the naturally occurring proteins (wild type and naturally occurring mutants) may be of use as reagents in a diagnostic assays for Alzheimer's disease. This does not provide a disclosure of how to use other variants, muteins or functionally conserved variants encompassed by the claims." As an extension, since other mammals do not get Alzheimer's disease, how then are these other mammalian proteins to be used ? Applicants' specific citation of page 12, line 12- page 13, line 1, page 13, line 11 - page 14, line 26 and pages 49-54 of the specification specifically supports diagnostic purposes of the human E5-1 wild type sequence SEQ ID NO:138 and specific mutations thereof for which the examiner has stated are enabled. However, these passages do not teach how to use the other mammalian E5-1 proteins claimed. Because other mammals do not get Alzheimer's disease, these proteins could not be used as diagnostics

reagents in other mammals. Thus, applicants arguments are not persuasive and the rejection is maintained.

Claim Objections

7. Claims 73, 75 and 76 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Status of Claims

8. Claims 24, 71, 74 and 77-79 are remain rejected.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310.

Patricia A. Duffy, Ph.D.
June 4, 1998

Patricia A. Duffy

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1640